

IN THE CLAIMS:

Please amend the claims as follows:

15. (Amended) A vector [for preparing] that confers [a] glutamine [independent] independence to a transformed [lymphoid] myeloma cell line comprising a GS gene and a gene or genes encoding a [protein] protein(s) heterologous to said [lymphoid] myeloma cell line, wherein the genes are arranged such that said GS gene can be expressed and glutamine independent myeloma colonies can be produced.

16. (Twice amended) The method of Claim 15, wherein said gene or genes encoding the [protein] protein(s) heterologous to said [lymphoid] myeloma cell line comprises a relatively strong promoter, and wherein said GS gene comprises a relatively weak promoter located upstream of said [the] gene or genes encoding the [protein] protein(s) heterologous to said [lymphoid] myeloma cell line so that transcription of the heterologous gene or genes does not run through the GS gene.

17. (Amended) The method of claim 15, wherein said gene or genes encoding the [protein] protein(s) heterologous to said [lymphoid] myeloma cell line comprises a relatively strong promoter, and wherein said GS gene comprises a relatively weak promoter that directs expression in the

*D#*  
*Comb*  
opposite direction to that of said gene or genes encoding the [protein] protein(s) heterologous to [lymphoid] said myeloma cell line.

*E* *6* *methal* *4*  
20. (Amended) The ~~vector~~ of claim 18, wherein said vector comprises a GS gene that comprises a weak promoter, and wherein said gene or genes encoding the [protein] protein(s) heterologous to said [lymphoid] myeloma cell line comprises an Ig heavy chain gene having a strong promoter and an Ig light chain gene having a strong promoter, wherein said strong promoter of said light chain gene is oriented in the opposite direction to said promoters of said GS and heavy chain genes, and wherein said Ig heavy chain gene is downstream from said GS gene.

*E* *7* *methal* *1*  
21. (Twice amended) The ~~vector~~ of Claim 15, wherein said vector comprises a GS gene that comprises a weak promoter, and wherein said gene or genes encoding the [protein] protein(s) heterologous to said [lymphoid] myeloma cell line comprises an Ig heavy chain gene having a strong promoter and an Ig light chain gene having a strong promoter, wherein said strong promoter of said Ig light chain gene is orientated in the opposite direction to said promoters of said GS and heavy chain genes, and wherein said Ig heavy chain gene is downstream from said GS gene so that

transcription of the heterologous gene does not run through the GS gene.

*D5 Cont*  
*8*  
22. (Twice amended) The *method* *1* vector of Claim 18, wherein said GS gene comprises a weak promoter, wherein said gene or genes encoding the [protein] protein(s) heterologous to said lymphoid cell line comprises an Ig light chain gene having a strong promoter and an Ig heavy chain gene having a strong promoter, wherein said GS gene, Ig light chain gene, and Ig heavy chain gene are transcribed in the same direction, and wherein said GS gene is located upstream of said Ig light chain gene and said Ig heavy chain gene so that transcription of the heterologous [gene] gene(s) does not run through the GS gene.

*C*  
Kindly add the following new claims:

*E* *9*  
23. The *method* *1* vector of claim 15 wherein the GS gene is expressed from an SV40 early region promoter.

*E* *10*  
24. The *method* *1* vector of claim 15 wherein the GS gene is expressed from an hCMV-MIE promoter.

*D6* *11*  
25. The *method* *9* vector of claim 23 wherein the GS gene and promoter are derived from pSV2GS.

E 12 method 10  
26. The vector of claim 24 wherein the GS gene and promoter are derived from pCMGS.

E 13 method 11  
27. The vector of claim 15 wherein all genes are expressed from the same type of promoter.

E 14 method 13  
28. The vector of claim 27 wherein the type of promoter is the hCMV-MIE promoter.

E 15 method 14  
29. The vector of claim 28 wherein the vector is derived from pCMGS.

D 16 method 8  
30. The vector of claim 22 wherein the vector is pSV2GScLccHc or pST6.

cont  
31. A method of selecting myeloma cells transfected with the vector of any of claims 15-30, comprising:

(i) plating transfected cells in non-selective medium containing glutamine;

(ii) after 24 hours, adding two volumes of glutamine-free medium; and

(iii) recovering myeloma colonies after 7 days incubation.

*E2*  
32. A vector that confers glutamine independence to a transformed lymphoid cell line, comprising a GS gene and a gene or genes encoding a protein(s) heterologous to said lymphoid cell line, wherein the genes are arranged such that said GS gene can be expressed and glutamine independent lymphoid colonies can be produced.

*D6 Cont*  
*E* <sup>19</sup> *method* <sup>18</sup>  
33. The ~~vector~~ of claim 32, wherein said gene or genes encoding the protein(s) heterologous to said lymphoid cell line comprises a relatively strong promoter, and wherein said GS gene comprises a relatively weak promoter located upstream of said gene or genes encoding the protein(s) heterologous to said lymphoid cell line so that transcription of the heterologous gene or genes does not run through the GS gene.

*E* <sup>20</sup> *method* <sup>19</sup>  
34. The ~~vector~~ of claim 33 wherein said relatively weak promoter is the SV40 early region promoter and said relatively strong promoter is the hCMV-MIE promoter.

*E* <sup>21</sup> *method* <sup>18</sup>  
35. The ~~vector~~ of claim 32 wherein said gene or genes encoding the protein(s) heterologous to said lymphoid cell line comprises a relatively strong promoter, and wherein said GS gene comprises a relatively weak promoter that directs expression in the opposite direction to that of said gene or

genes encoding the protein(s) heterologous to said lymphoid cell line.

*22*  
36. The ~~vector~~<sup>method</sup> of claim ~~35~~<sup>21</sup> wherein said relatively weak promoter is the SV40 early region promoter and said relatively strong promoter is the hCMV-MIE promoter.

*23*  
37. The ~~vector~~<sup>method</sup> of claim ~~35~~<sup>21</sup>, wherein said vector comprises a GS gene that comprises a weak promoter, and wherein said gene or genes encoding the protein(s) heterologous to said lymphoid cell line comprises an Ig heavy chain gene having a strong promoter and an Ig light chain gene having a strong promoter, wherein said strong promoter of said light chain gene is oriented in the opposite direction to said promoters of said GS and heavy chain genes, and wherein said Ig heavy chain gene is downstream from said GS gene.

*Def Cont*

*24*  
38. The ~~vector~~<sup>method</sup> of claim ~~32~~<sup>18</sup>, wherein said vector comprises a GS gene that comprises a weak promoter, and wherein said gene or genes encoding the protein(s) heterologous to said lymphoid cell line comprises an Ig heavy chain gene having a strong promoter and an Ig light chain gene having a strong promoter, wherein said strong promoter of said Ig light chain gene is orientated in the opposite

direction to said promoters of said GS and heavy chain genes, and wherein said Ig heavy chain gene is downstream from said GS gene so that transcription of the heterologous gene does not run through the GS gene.

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30. The ~~vector~~ <sup>method</sup> of Claim 32, wherein said GS gene comprises a weak promoter, wherein said gene or genes encoding the protein(s) heterologous to said lymphoid cell line comprises an Ig light chain gene having a strong promoter and an Ig heavy chain gene having a strong promoter, wherein said GS gene, Ig light chain gene, and Ig heavy chain gene are transcribed in the same direction, and wherein said GS gene is located upstream of said Ig light chain gene and said Ig heavy chain gene so that transcription of the heterologous gene(s) does not run through the GS gene.--

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D6  
Cont

#### REMARKS

The Examiner's Action mailed August 27, 1996, has been received and its contents carefully noted.

The specification has been amended to correct the continuity information for the present application, and to correct the description on page 16, line 37, of pSV2GScLc, in which the GS gene is under control of the SV40 early region promoter. Support for this correction can be found in Figure 2, page 10, lines 9-11, and page 8, lines 19-21.